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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,690	05/11/2001	John Tane Christeller	020829-000100US	7473

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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 03/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,690	CHRISTELLER ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-23,31 and 53-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-23,31 and 53-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 December 2003 has been entered.

2. Claims 16-23, 31 and 53-65 are pending.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

4. Claim 65 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for the phrases "biotin carboxyl carrier protein" and "seed biotin-binding protein". Thus, such a phrases constitute NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrases or to cancel the new matter.

5. Claims 16-23, 31 and 53-64 remain rejected and claim 65 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the

time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 21 August 2003, as applied to claims 16-23, 31 and 53-64. Applicant's arguments and the Declaration of Dr Christeller, both filed 22 December 2003, have been fully considered but they are not persuasive.

Applicant urges that MPEP 2173.02 states that definiteness must be analyzed in light of the specification, teachings of the prior art and level of ordinary skill in the art (response pg 8).

This is not found persuasive because MPEP 2173.02 is directed to 35 U.S.C. 112 second paragraph rejections.

Applicant urges that one of skill in the art could readily determine the structural features and physical properties of suitable vacuole targeting sequences and biotin binding sequences and functionally equivalent variants or fragments thereof (response pg 8).

This is not found persuasive because the written description requirement means that it is the specification must describe the nucleic acids encoding the suitable vacuole targeting sequences and biotin binding sequences and functionally equivalent variants or fragments thereof.

Dr Christeller states that based on the knowledge in the filed, one of skill in the art would be able to determine the structural and functional characteristics of vacuole targeting sequence and biotin binding sequences (Declaration ¶7).

This is not found persuasive because the specification must describe such sequences.

Dr Christeller states that vacuole targeting sequences are those that target a protein to the vacuole and lists a number of them in Appendix C; one of skill in the art could readily obtain or make such sequences (Declaration ¶7-8).

This is not found persuasive. The references in Appendix C could not considered because they were not sent. However, it is noted that a number of the references appear to have been published after the filing date of the instant application, and thus cannot provide written description support for the instant application. The specification does not describe the majority of these sequences.

Dr Christeller states that one of skill in the art could confirm the suitability of candidate vacuole targeting sequences through known means and techniques, for example by homology comparison or experimentation to confirm vacuole targeting using a reporter gene, citing Gallagher and Hicks (Declaration ¶9).

This is not found persuasive. This is an argument against an enablement rejection, and will be addressed below. Gallagher and Hicks could not considered because they were not sent.

Dr Christeller states that a biotin binding sequence is a protein that binds biotin and lists a number of biotin binding proetins in Appendices D and E; one of skill in the art could readily obtain or make such sequences (Declaration ¶7 and 10).

This is not found persuasive. The references in Appendices C and D could not considered because they were not sent. However, it is noted that a number of the references appear to have been published after the filing date of the instant application, and thus cannot provide written description support for the instant application. Additionally, it does not appear that these references describe the sequence of many of these proteins (*e.g.*, the biotin-binding antibodies, the proteins in the references published in the 1970's and early 1980's, all the proteins in serum, and functionally equivalent variants and fragments of all these and the other recited proteins).

Dr Christeller states that one of skill in the art could confirm the suitability of candidate biotin binding sequences through known means and techniques, for example by homology comparison or experimentation to confirm biotin binding, citing Wilcheck et al and references therein (Declaration ¶11).

This is not found persuasive. This is an argument against an enablement rejection, and will be addressed below. Wilcheck et al and references therein could not considered because they were not sent.

Dr Christeller states that the structural and physical characteristics of the reported or putative vacuole targeting or biotin binding sequence could be determined by one of ordinary skill in the art using known sequence techniques and algorithms, citing Emanuelsson et al, and that nucleic acid sequence could be constructed from amino acid sequences (Declaration ¶12).

This is not found persuasive. The specification must describe the structural features (*i.e.*, the sequence) of the claimed nucleic acids, and it does not. Emanuelsson et al could not considered because it was not sent.

Dr Christeller states that none of this analysis would constitute undue experimentation (Declaration ¶13).

This is not found persuasive. This is an argument against an enablement rejection, and will be addressed below.

6. Claims 16-23, 31 and 53-64 remain rejected and claim 65 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids that encode a chimeric protein comprising any vacuole targeting sequence operably linked to avidin or streptavidin, cells and plants transformed with those nucleic acids, and methods of using the

cells and plants to produce the protein, does not reasonably provide enablement for nucleic acids that encode a chimeric protein comprising any vacuole targeting sequence operably linked to any biotin-binding sequence, or functional variants or fragments thereof or nucleic acids comprising a vacuole targeting sequence operably linked to any biotin-binding sequence, or functional variants or fragments thereof, cells and plants transformed with those nucleic acids, and methods of using the cells and plants to produce the protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 21 August 2003, as applied to claims 16-23, 31 and 53-64. Applicant's arguments and the Declaration of Dr Christeller, both filed 22 December 2003, have been fully considered but they are not persuasive.

Applicant urges that experimentation is permitted, as long as that experimentation is not undue, and a claim can be broad as long as one can determine any one of the claimed embodiments, citing MPEP 2164.01 and 2164.08 (response pg).

This is not found persuasive. The claimed nucleic acids must be taught within the full scope of the claims. In the instant case, they are not. Biotin-binding proteins, and the nucleic acids that encode them, are not taught within the full scope of the claims. For example, the sequences of antibodies that bind biotin are not taught.

Applicant urges that specification provides guidance by defining biotin binding sequences and their functional equivalents as forming a complex with a specific dissociation constant, describes several such sequences on pg 13-14, and provides working examples (response pg 10).

This is not found persuasive. A definition of a sequence does not teach the sequence itself. The sequence of biotin-binding antibodies is not taught, for example. Additionally, not all serum proteins bind biotin, and anyway, the specification does not teach the sequence of all serum proteins, much less all the biotin-binding ones.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at pg 1027

> ... despite extensive statements in the specification concerning all the analogs of the EPO gene that can be made, there is little enabling disclosure of particular analogs and how to make them. Details for preparing only a few EPO analog genes are disclosed. Amgen argues that this is sufficient to support its claims; we disagree. This "disclosure" might well justify a generic claim encompassing these and similar analogs, but it represents inadequate support for Amgen's desire to claim all EPO gene analogs. There may be many other genetic sequences that code for EPO-Type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them.

Dr Christeller states that vacuole targeting sequences are those that target a protein to the vacuole and lists a number of them in Appendix C; one of skill in the art could readily obtain or make such sequences (Declaration ¶7-8).

This is not found persuasive. The references in Appendix C could not considered because they were not sent. However, it is noted that a number of the references appear to have been published after the filing date of the instant application, and thus cannot provide written description support for the instant application. The specification must teach how to make these sequences, and the instant specification does not.

See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Dr Christeller states that one of skill in the art could confirm the suitability of candidate vacuole targeting sequences through known means and techniques, for example by homology

comparison or experimentation to confirm vacuole targeting using a reporter gene, citing Gallagher and Hicks (Declaration ¶9).

This is not found persuasive. The specification must teach how to make, not how to find, the claimed nucleic acids; the specification does not do so. Gallagher and Hicks could not considered because they were not sent.

Dr Christeller states that a biotin binding sequence is a protein that binds biotin and lists a number of them in Appendices D and E; one of skill in the art could readily obtain or make such sequences (Declaration ¶7, 10, 18 and 21).

This is not found persuasive. The references in Appendices C and D could not considered because they were not sent. However, it is noted that a number of the references appear to have been published after the filing date of the instant application, and thus cannot provide written description support for the instant application. Additionally, some of the references appear to teach isolation of the protein but not its sequence or the sequence of the nucleic acid that encodes it. The specification must teach how to make, not how to find, the claimed nucleic acids; the specification does not do so.

Dr Christeller states that one of skill in the art could confirm the suitability of candidate biotin binding sequences through known means and techniques, for example by homology comparison or experimentation to confirm biotin binding, citing Wilcheck et al and references therein (Declaration ¶11).

This is not found persuasive. The specification must teach how to make, not how to find, the claimed nucleic acids and the starting materials for the claimed methods. Wilcheck et al and references therein could not considered because they were not sent.

Dr Christeller states that the structural and physical characteristics of the reported or putative vacuole targeting or biotin binding sequence could be determined by one of ordinary skill in the art using known sequence techniques and algorithms, citing Emanuelsson et al, and that nucleic acid sequence could be constructed from amino acid sequences (Declaration ¶12).

This is not found persuasive. The specification must teach how to make, not how to find, the claimed nucleic acids; the specification does not do so. Emanuelsson et al could not considered because it was not sent.

Dr Christeller states that none of this analysis would constitute undue experimentation (Declaration ¶13).

This is not found persuasive because given the lack of guidance as to the sequence of nucleic acids that encode biotin-binding proteins and the lack of guidance as to which amino acids to modify or which fragments would also bind biotin, undue trail and error experimentation would be required to practice the invention within the full scope of the claims, if such practice were even possible.

Dr Christeller states that one of skill in the art would interpret the language of the present claims to exclude variants and fragments that do not bind biotin, and would interpret variants and fragments as sequences that are varied in some way from or are portions of biotin binding sequences (Declaration ¶17).

This is not found persuasive because the specification does not teach how to make variants and fragments that are functional, versus ones that are not.

Dr Christeller states that the specification teaches plant transformation and appendix F lists a number of such protocols (Declaration ¶23).

This is not found persuasive because the rejection is not drawn to plants transformation, but to the DNAs used in that transformation.

Dr Christeller states that examples 4-6 teach preferred methods of testing plants for the presence of an expressed biotin binding sequence, correct targeting to the vacuole and toxicity (Declaration ¶24).

This is not found persuasive. Again, the rejection is drawn to lack of enablement for nucleic acids that encode a chimeric protein comprising any vacuole targeting sequence operably linked to any biotin binding sequence or a variant or fragment thereof, or nucleic acids comprising a vacuole targeting sequence operably linked to any biotin-binding sequence, or functional variants or fragments thereof; the claimed method of plant transformation is not enabled because the nucleic acids used in the method are not taught, not because plant transformation itself is not taught or well-known in the art.

7. Claims 16-23, 31 and 53-64 remain rejected and claim 65 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is modified from the rejection set forth in the Office action mailed 21 August 2003, as applied to claims 16-23, 31 and 53-64. Applicant's arguments filed 22 December 2003 have been fully considered but they are not persuasive.

Claim 16 is indefinite for its recitation of "functionally equivalent variant". It is unclear what function is equivalent, and it is unclear how the sequence of the variant differs from that of the biotin binding sequence.

Applicant urges that variant is defined on pg 12, lines 3-8 (response pg 12).

This is not found persuasive. The specification on pg 12, lines 3-8 states:

> "The term 'variant' as used herein refers to a polypeptide wherein the amino acid sequence exhibits substantially 70% or greater homology with the amino acid sequences set out in Figures 1 and 4. Presumably, the variants will have greater than 85% homology, and, most preferably, 95% homology or more. Variants may be arrived at by modification of the native amino acid sequence by such modifications as insertion, substitution or deletion of one or more amino acids."

Fig. 1 shows a portion of the nucleic acid sequence for potato proteinase inhibitor I and Fig. 4 shows a portion of the nucleic acid sequence for potato proteinase inhibitor II.

As no amino acid sequences are set out in Figs 1 and 4, the definition is meaningless. Furthermore, even if Figs 1 and 4 showed the amino acid sequences of potato proteinase inhibitors I and II, the definition would still be meaningless, because 1) these proteins are not biotin-binding proteins and thus cannot be functionally equivalent to one, unless the function is not biotin binding, and 2) it is unclear what 70% "homology" means as "homology" is not defined - does it mean identical or are certain substitutions (*e.g.*, conservative ones) included?

The following rejections are new, due to amendment:

It is unclear in claims 21 and 31, what polypeptide is being produced, as any nucleic acid molecule has multiple open reading frames.

Claim 65 lacks antecedent basis for the limitation "the nucleic acid sequence of claim 16" as claim 16 is drawn to a nucleic acid molecule.

Conclusion

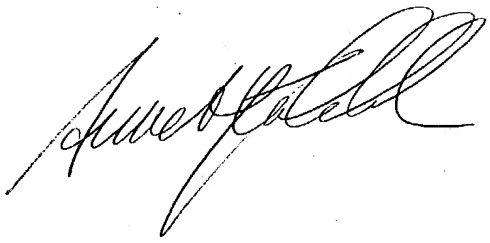
8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (571) 272-1600.

Anne R. Kubelik, Ph.D.
March 1, 2004



ANNE KUBELIK
PATENT EXAMINER